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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/783,619	02/20/2004	Ming Chiu Fung	14761US02	7207

40614 7590 06/25/2007

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EXAMINER	
MI, QIUWEN	
ART UNIT	**PAPER NUMBER**
1655	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/783,619	FUNG ET AL.	
	Examiner	Art Unit	
	Qiuwen Mi	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *72-100* is/are pending in the application.

4a) Of the above claim(s) *83-86 and 97-100* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *72-82 and 87-96* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment in the reply filed on 5/31/07 is acknowledged. Any rejection that is not reiterated is hereby withdrawn.

Newly submitted claims 83-86, and 97-100 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claims 72-82, and 87-96 are drawn to a composition; claims 83-86, and 97-100 are drawn to a method of treating hemoglobinopathies. Inventions of claims 72-82, and 87-96 and claims 83-86, and 97-100 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case claims 83-86, and 97-100 can be used in a materially different process, such as treating cancer.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 83-86, 97-100 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims Pending

Claims 1-71 are cancelled. Claims 72-100 are newly submitted. Claims 72-100 are pending. Claims 83-86, and 97-100 are withdrawn. Claims 72-82, and 87-96 are examined on the merits.

Claim Rejections –35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 87, and 89-92 are rejected under 35 USC § 102 (a) as being anticipated by Oh et al (Planta Med 68: 832-833, 2002).

Oh et al teach that the dried roots of *Trichosanthes kirilowii* Maxim were extracted with MeOH. The MeOH extract was concentrated (heat and form a syrup), suspended in water, and sequentially partitioned with n-hexane (a second solvent having a polarity index less than MeOH), EtOAc, and BuOH. The bioactive EtOAC fraction (a second solvent having a polarity index less than MeOH) (second syrup) was subjected to column chromatography. The final product cucurbitacin D (in EtOH, pharmaceutically acceptable carrier) was purified from NP-HPLC (page 833, left column, third paragraph).

Therefore, the reference is deemed to anticipate the instant claim above.

Claim Rejections –35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior

art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 72-82, and 87-96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Iketani et al (JP 62108844) in view of Ozaki et al (Biological & pharmaceutical bulletin, (1996 Aug) Vol. 19, No. 8, pp. 1046-8), and further in view of Oh et al (Planta Med 68: 832-833, 2002).

Iketani et al (JP 62108844, see the full translation attached) teach that *Trichosanthes* seeds including the dried seeds of *Trichosanthes kirillowii* etc are extracted by heating to between 0 °C and a temperature at or below the boiling point of the solvent using one or more solvents selected from water, ethanol (boiling temperature 78 °C, thus between 40-80 °C), etc individually, or as a mixed solvent to obtain a liquid extract. This liquid extract is applied to column chromatography as is or by concentrating or drying it (page 3, 5th paragraph; page 4, first paragraph). The eluate is fractionated to obtain a crude fraction, and water, ethanol, ethyl acetate, ether, chloroform, etc can be used individually for the elution solvent (page 4, first paragraph). Iketani et al also teach applying crude fraction to high-speed liquid chromatography and use mobile phase acetonitrile/tetrahydrofuran/water (page 6, second paragraph), and a formulation comprising a pharmaceutical excipient (carrier or adjuvant) (page 15, 4th paragraph).

Iketani et al do not teach species *Trichosanthes rosthornii* or *Trichosanthes japonica*, the exact HPLC conditions in claims 75 and 88, a second solvent with less polarity than the first solvent, do not explicitly teach using 50-70% ethanol as a first solvent, ethanol as a second solvent with a polarity index less than the first solvent.

Ozaki et al teach the anti-inflammatory effect of 50% ethanol (polarity index 5.2) extract obtained from the fruit of *Trichosanthes kirilowii* (see the Abstract).

Oh et al teach that the dried roots of *Trichosanthes kirilowii* Maxim were extracted with MeOH. The MeOH extract was concentrated (heat and form a syrup), suspended in water, and sequentially partitioned with n-hexane (a second solvent having a polarity index less than MeOH), EtOAc, and BuOH. The bioactive EtOAC fraction (a second solvent having a polarity index less than MeOH) (second syrup) was subjected to column chromatography. The final product cucurbitacin D (in EtOH, pharmaceutically acceptable carrier) was purified from NP-HPLC (page 833, left column, third paragraph).

Therefore, it would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to use 50-70% ethanol or ethanol from Ozaki et al to extract *Trichosanthes rosthornii* or *Trichosanthes japonica*, a second solvent with less polarity than the first solvent from Oh et al, and the right condition to isolate the effective component from HPLC for the following reasons.

It is taught by Iketani et al that genus *Trichosanthes* seeds can be extracted with water, ethanol, etc individually, or as a mixed solvent to obtain a liquid extract. A mixture of water and ethanol is a well known solvent in the art for plant extraction, plus Ozaki et al teach that the 50% ethanol extract obtained from the fruit of *Trichosanthes kirilowii* has anti-inflammatory effect, therefore it would have been *prima facie* obvious for one of ordinary skill in the art at the time

the invention was made to use 50-70% ethanol or ethanol to extract the two species *Trichosanthes rosthornii* or *Trichosanthes japonica* in genus *Trichosanthes*. Since Ozaki et al teach that the 50% ethanol extract obtained from the fruit of *Trichosanthes kirilowii* has anti-inflammatory effect, one of ordinary skill in the art would have been motivated to make the modifications.

It is clear from Oh et al that using a second solvent with less polarity than the first solvent resulted in the isolation of an effective skin depigmentation component from *Trichosanthes kirilowii* that effectively inhibites melanin synthesis through tyrosinase (see Abstract, page 832, right column, second paragraph). Therefore, it would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to use a second solvent with less polarity than the first solvent to extract the plant. Since Oh et al provide the beneficial scientific data, one of ordinary skill in the art would have been motivated to make the modifications.

The combination of water, acetonitrile, and trifluoroacetic acid (or any other acid/base for pH adjustment according to the acidity of the effective component) is a routine HPLC mobile phase, and Iketani et al teach the combination of water and acetonitrile (page 6, second paragraph) in the reference. The result-effective adjustment in conventional working parameters (e.g., determining an appropriate concentration of mobile phase to purify the *Trichosanthes* extract) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Qiuwen Mi whose telephone number is 571-272-5984. The examiner can normally be reached on 8 to 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MICHAEL MELLER
PRIMARY EXAMINER